REMARKS

Reconsideration of the outstanding objections and rejections raised in the Office Action mailed April 7, 2011 (hereinafter, "Office Action") is respectfully requested. Claims 40-42 and 48-51 were previously pending in this application. Claims 40-42 and 48-50 are amended herein. Support for the amendments may be found, for example, at page 22, lines 16-32 of the original application. No new matter is being introduced by way of amendment.

Rejections Under 35 U.S.C. § 112

Claims 40-42 and 48-51 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Office Action at 4 and 14. Claim 40 is rejected as being indefinite for lacking sufficient antecedent basis for the claim limitation "extracellular fluid." *Id.* at 14. Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, claim 40 is amended to recite "the extracellular fluid" as suggested by the Examiner.

Claim 41 is rejected as being indefinite for lacking sufficient antecedent basis for the claim limitation "extracellular fluid" in line 2 and "gelsolin" in the last line. *Id.* at 4. Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, claim 41 is amended to recite "the extracellular fluid" as suggested by the Examiner. Claim 41 is also amended to clarify that the comparison is to a level of gelsolin obtained from the patient subject before administration.

Claim 42 is rejected as being indefinite for lacking sufficient antecedent basis for the claim limitation "platelets." *Id.* at 5 and 14. Claim 42 is amended to recite "the platelets" as suggested by the Examiner.

Claims 48 and 50 are rejected as being indefinite about what is being conveyed with the term "comprises." *Id.* at 14. Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, claims 48 and 50 are amended. Claim 48 is amended to recite that the gelsolin is plasma gelsolin, or a functionally equivalent peptide fragment thereof. Claim 50 is amended to recite that the gelsolin is recombinantly produced or expressed gelsolin, or a functionally equivalent peptide fragment thereof.

Claim 49 is rejected as being indefinite in the limitation "comprises amino acid residues

160-169 of gelsolin." *Id.* at 15. Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, claim 49 is amended to specify amino acid residues 160-169 of "the gelsolin" as suggested by the Examiner.

Claims 41, 42, and 48-51 are rejected for depending from an indefinite base claim. *Id.* at 15. The base claim, claim 40, as amended herein is not indefinite.

In view of the amendments herein, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112.

Rejections Under 35 U.S.C. § 102

Claims 40-42 and 51 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Rosen *et al.* (WO 00/55350A1) as evidenced by Janmey *et al.* (*J. Biol. Chem.* 267:11818-11823, 1992) and Sheu *et al.* (*Brit. J. Hematol.* 103: 29-38, 1998). The Examiner asserts that Rosen *et al.* "taught each and every structural element of the claims in complete detail, expressly or inherently, and therefore anticipate the claimed invention." Office Action at 7. The Examiner states that it "is unclear what do Applicants mean by the statement that the claim is directed to a combination of elements, because the instant claims are not directed to a combination of elements." *Id.* at 7.

Applicant respectfully traverses this rejection. As currently amended, the claims are directed to a method comprising administering to the blood or the extracellular fluid of a patient in need of an increased concentration of gelsolin, a therapeutically effective amount of gelsolin or a functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of the platelets in the blood or the extracellular fluid of the patient. Rosen *et al.* do not teach the instant claims.

As explained in the response filed on January 24, 2011, Rosen *et al.* do not teach the *specific claimed combination* (combination of particular polypeptide(s) and/to particular condition(s)) and do not show the instant invention in as complete detail as is contained in the claim. Rosen *et al.* disclose hundreds of cancer associated polypeptides and allege that the disclosed cancer associated polypeptides can be used to treat various diseases or conditions out of a long list of examples of diseases and conditions. Polypeptide of SEQ ID NO: 1065 is one of 842 human cancer associated polypeptides, and infectious diseases is one of the long list of medical conditions disclosed in Rosen

et al. Rosen *et al.* do not teach or provide any direction to one of ordinary skill in the art as to which polypeptide(s) is/are therapeutically effective for which disease(s) or condition(s). More particularly, Rosen *et al.* do not specifically teach using gelsolin or polypeptide of SEQ ID NO: 1065 to treat any particular condition, let alone LPS-induced generalized coagulation dysfunction.

The Court of Appeals for the Federal Circuit ("CAFC") has repeatedly held that for a reference to anticipate under 35 U.S.C. §102, the reference must not only disclose all the elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim." A reference cannot be alleged to prove prior invention of a claimed subject matter and cannot anticipate under 35 U.S.C. §102 unless the reference discloses within the four corners of the document not only all of the limitations of the claimed invention, but also all of the limitations arranged or combined in the same manner as recited in the claim, not merely in a particular order. Net MoneyIn v. Verisign, 545 F.3d 1359 (Fed. Cir. 2008). The reference must clearly and unequivocally disclose the claimed invention or direct a person of skill in the art to the invention without there being any need to pick, choose and combine various teachings of the cited reference. In re Arkley, 455 F.2d 586 (C.C.P.A. 1972). Rosen *et al.* merely recite individual elements as part of long lists of possibilities without any suggestion or guidance leading one of ordinary skill in the art to make the specific combination claimed, as opposed to any other of a long list of alternative possibilities or myriad of possible combinations. In making the rejection, the Examiner picks, chooses and combines various teachings from throughout Rosen *et al.* (Claim 17, the 'Infectious Disease' section at pages 403, 371, 372, 374, 375, 384, and 395, and to the 'Therapeutic/Prophylactic Administration and Composition' section at pages 336, 405 and 406, and 1051-1054) to allegedly arrive at the instant claims. As stated above, Rosen *et al.* do not specifically teach using polypeptide of SEQ ID NO: 1065 to treat any particular condition, let alone LPS-induced generalized coagulation dysfunction. Thus, Rosen *et al.* do not clearly and unequivocally disclose the claimed invention and do not direct a person of skill in the art to the invention without there being a need to pick, choose and combine various teachings of the cited reference. Therefore, Rosen *et al.* is not sufficient as an anticipatory reference.

The Examiner cites case law relating to inherency and indicates, for example, "That the polypeptide…representing amino acids 29-48 of the prior art SEQ ID NO: 1065 represents a

biologically active gelsolin or a functionally equivalent peptide fragment of gelsolin and comprises Applicants' SEQ ID NO: 1 is inherent for the teachings of Rosen *et al.* in light of what is known in the prior art…Since the prior at gelsolin sequence is that same as Applicants' gelsolin sequence, it necessarily possesses the same function as that of the Applicants' gelsolin sequence." Office Action at 9. It is noted, again, that Rosen *et al.* discloses SEQ ID NO: 1065 among hundreds of polypeptides and makes no direct connection between this peptide and its capacity to maintain or restore normal aggregation of platelets, particularly a therapeutically effective amount of SEQ ID NO: 1065 that would maintain or restore normal aggregation of platelets. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). Rosen *et al.* do not disclose gelsolin in a therapeutically effective amount, *e.g.*, in an amount effective to restore or maintain normal aggregation of platelets. This element of the instant claims does not necessarily flow from the teachings of Rosen *et al.* Thus, the Examiner cannot rely upon the theory of inherency to reject the instant claims.

The Examiner asserts that "with regard to Applicants' argument that Rosen et al. disclose hundreds of cancer associated polypeptides and that the disclosed cancer associated polypeptides can be used to treat various diseases or conditions out of a long list of examples of diseases and conditions [Applicant had cited *Minnesota Mining and Manufacturing Company v. Johnson & Johnson Orthopedics, Inc.* 976 F.2d 1559, 1572 (Fed. Cir. 1992) in support of the argument], the following must be noted. A species which is specifically disclosed in a prior art reference is anticipatory even though it appears 'without special emphasis in a longer list.' Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1376 (Fed. Cir. 2005)." Office Action at 10.

In Perricone, the prior art patent ("Pereira") cited against the Perricone patents (relating to, *e.g.*, methods of preventing skin disorders by topical application of ascorbyl fatty acid ester (active ingredient)) listed 13 other ingredients in addition to the active ingredient. The Pereira patent also disclosed specific concentrations of the active ingredient within or overlapping with the ranges claimed by the Perricone patents. The court rejected "the notion that one of these ingredients cannot anticipate because it appears without special emphasis in a longer list." *Perricone* at 1376. The

court concludes its reasoning, "[t]o the contrary, the disclose is prior art to the extent of its *enabling disclosure*. See Hewlet-Packard Co. v. Mustek Sys., Inc., 340 F.3d 1314, 1324 n.6 (Fed Cir. 2003) (emphasis added). In sum, the Pereira patent may be considered to anticipate the methods of the Perricone patents to the extent that the Pereira patent has an enabling disclosure.

Even assuming, for argument's sake, that Rosen *et al.* teach polypeptide of SEQ ID NO: 1065 to treat coagulation disorders, which Applicant clearly disagrees with for the reasons outlined above, Rosen *et al.* is not an *enabling disclosure* for administering to the blood or the extracellular fluid of a patient in need of an increased concentration of gelsolin, a therapeutically effective amount of gelsolin, or a functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient.

An anticipatory reference must provide an enabling disclosure of the desired subject matter, and mere naming or description of the subject matter is insufficient. "A reference contains an 'enabling disclosure' if the public was in possession of the claimed invention before the date of invention. 'Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention.' In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985)" MPEP § 2121.01. One of skill in the art could not have combined the description of Rosen *et al.* with his or her own knowledge to make the claimed invention because, prior to the instant invention, one of ordinary skill in the art would not have known of the correlation between a polypeptide comprising SEQ ID NO: 1065 or gelsolin and the restoration or maintenance of normal platelet aggregation, let alone a therapeutically effective amount of a polypeptide comprising SEQ ID NO: 1065 or gelsolin that would restore or maintain normal aggregation of platelets.

The Examiner further cites various court cases relating to compound claims, particularly pointing out that if a compound is recited in a reference, even among a list of other compounds, that reference is an anticipatory reference to that compound. Office Action at 13.

The instantly claimed subject matter are methods, not compounds. Applicant is not claiming gelsolin.

The Examiner asserts that "merely discovering and claiming a new benefit of an old process cannot render the process again patentable. In re Woodruss, 16 USPQ2d 1934, 1936 (Fed. Cir.

1990)." *Id.* The instant claims are directed to a novel method and not to a new benefit of an old process. The instantly claimed method(s) for restoring or maintaining normal aggregation of platelets in blood or extracellular fluid of a patient subject to or susceptible to LPS-induced generalized coagulation dysfunction, said method comprising administering to the blood or the extracellular fluid of a patient in need of an increased concentration of gelsolin, an effective amount of gelsolin, or a functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient is a novel method that is not described or suggested in the prior art.

In view of the foregoing, Rosen *et al.* do not anticipate the instant claims. Accordingly, withdrawal of the rejection of the claims under 35 U.S.C. § 102(b) is respectfully requested.

Claims 40-42 and 48-51 are rejected under 35 U.S.C. §102(b) as being anticipated by Rothenbach *et al.* (*J. Appl. Physiol.* 96: 25-31, January 2004, first published May 2, 2003) as evidenced by Janmey *et al.* (*J. Biol. Chem.* 267:11818-11823, 1992).

In reference to Rothenbach *et al.*, the Examiner contends that "[s]ince the prior art product administered in to [sic] the blood of the patients susceptible to LPS-generalized coagulation dysfunction and the product administered in the instantly claimed method to a patient susceptible to LPS-generalized coagulation dysfunction is the same, i.e., gelsolin both administered in a therapeutically effective amount, it necessarily possesses the same function as that of Applicants' gelsolin sequence, i.e., the capacity to maintain or restore normal aggregation of platelets." Office Action at 17.

Applicant respectfully disagrees. Claim 40 as currently amended is directed to administering to the blood or the extracellular fluid of a patient in need of an increased concentration of gelsolin a therapeutically effective amount of gelsolin, or a functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient. Rothenbach *et al.* do not anticipate the claims as currently amended because Rothenbach *et al.* do not teach each and every limitation of the claimed invention. Rothenbach *et al.* do not expressly teach a correlation between plasma gelsolin levels and platelet aggregation. Rothenbach *et al.* do not teach or suggest administering gelsolin to a patient in an

amount effective to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient.

Rothenbach *et al.* investigated the role of plasma gelsolin in the pathophysiology of inflammation-induced lung injury (Abstract). Rothenbach *et al.* utilized a standardized rat burn model to induce a defined pulmonary injury and found that plasma gelsolin depletion contributes to the pathophysiology of pulmonary vascular dysfunction. Even if the animals used in their study were subject to or susceptible to LPS-induced generalized coagulation dysfunction, there is no teaching in the Rothenbach *et al.* reference to administer gelsolin in an amount that effectively restores or maintains normal aggregation of platelets in the blood or extracellular fluid of the patient. Rothenbach *et al.* do not teach a correlation between plasma gelsolin levels and restoration of platelet aggregation. Thus, Rothenbach *et al.* do not teach every element of the claimed invention and cannot be used as a prior art reference under 35 U.S.C. §102(b).

Reconsideration and withdrawal of the rejection of claims 40-42 and 48-51 under 35 U.S.C. §102(b) in view of Rothenbach *et al.* are respectfully requested.

Claims 40-42 and 48-51 are rejected under 35 U.S.C. §102(b) as being anticipated by Pepinsky *et al.* (WO 91/17170).

The Examiner asserts that Pepinsky *et al.* is an anticipatory reference because "Pepinksy et al. taught a method for treating a patient having ARC, HIV infection, or AIDS (i.e., a subject susceptible to LPS-induced generalized coagulation dysfunction) comprising administering to the patient a therapeutically effective amount of a multimeric recombinant fusion composition comprising gelsolin moiety, having anti-coagulant or clot-dissolving activity, i.e., inhibition of platelet aggregation or maintenance of normal platelet aggregation. The gelsolin moiety used was human plasma gelsolin, or a biologically active fragment containing amino acids 160 to 169 of Applicants' SEQ ID NO: 1." Office Action at 18.

Applicant respectfully disagrees. Pepinsky *et al.* do not anticipate the instant claims because Pepinsky *et al.* do not teach each and every limitation of the claimed invention. Pepinsky *et al.* do not teach a correlation between plasma gelsolin levels and platelet aggregation. Pepinsky *et al.* do

not teach or suggest administering gelsolin to a patient in an amount effective to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient.

The teachings of Pepinsky *et al.* relate to hetero-multimeric fusion constructs that can be targeted to particular antigens, for example, targets of the HIV virus. When targeted in this manner, multimeric gelsolin fusion constructs may be useful in blocking the binding of HIV to cells, thereby preventing infection. These multimeric fusion constructs comprise a gelsolin moiety for binding to polyphosphoinosides and comprise a functional moiety, for example, for targeting the fusion protein to particular antigens (Summary of the Invention). Pepinsky *et al.* do not teach administering to the blood or the extracellular fluid of a patient in need of an increased concentration of gelsolin a therapeutically effective amount of gelsolin, or a functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of platelets. Pepinsky *et al.* do not teach a correlation between plasma gelsolin levels and restoration of platelet aggregation. Thus, Pepinsky *et al.* do not teach every element of the claimed invention and cannot be cited as a prior art reference under 35 U.S.C. §102(b).

Reconsideration and withdrawal of the rejection of claims 40-42 and 48-51 under 35 U.S.C. §102(b) in view of Pepinsky *et al.* are respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. B0801.70356US01.

Dated: October 7, 2011

Respectfully submitted,

By_____

Roque El-Hayek
Registration No.: 55,151
Heather J. DiPietrantonio
Registration No.: 65,843
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000